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CONTRIBUTION ON THE THERAPY OF SYSTEMIC LUPUS ERYTHEMATOSUS WITH A COMBINATION OF CYCLOPHOSPHAMIDE (ENDOXAN) AND CORTICOSTEROIDS

E. Muhl, A. Adorf

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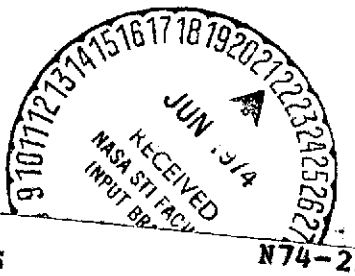

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16. Abstract

The article describes the course of a systemic Lupus erythematosus of a 27-year old female in which, after negative results with the methods of treatment customarily used up to now, first a combined therapy of corticosteroids with a cytostat (Endoxan) brought a decisive turn in the course of the disease and a hardly-expected result. The period of observation of this case extended over ten months, with initially 3 months of stationary treatment and, thereafter, 7 months of ambulatory treatment.

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CONTRIBUTION ON THE THERAPY OF SYSTEMIC LUPUS ERYTHEMATOSUS WITH A COMBINATION OF CYCLOPHOSPHAMIDE (ENDOXAN) AND CORTICOSTEROIDS

by E. Muhl, A. Adorf

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(Chief Physician: Dr. A. Adorf)

In spite of great progress in the diagnosis and the therapy /366* of the diseases of the 'rheumatic circle,' many problems are still unsolved. The clinical physicians,as well as also especially the immunobiologists, are concerning themselves at this time to a greatly enlarged degree, as to whether we have recognized that here, as in a series of other up to now etiologically obscure causes of disease, immunobiological or immunopathological processes play a possibly decisive role.

To the systemic diseases of connective tissue, we have long assigned the systemic Lupus erythematosus, sometimes also called 'collagenosis,' not entirely correctly, although we know,in the meantime,that the collagen fibers of the connective tissue are not primarily pathologically altered.

The clinical picture of this disease has many ramifications. The manifestation in the individual organs can be expressed in very different ways. Often in the foreground is the typical skin change that gave the disease form its name, sometimes involving attack on the joints,as in chronic poly-arthritis; sometimes the skin changes are like those of scleroderma, and an attack occurs on the arterial vessel system,as in the Raynaud syndrome,

*Numbers in the margin indicate pagination in the foreign text.

or in the periarteritus nodosa as also in giant cell arteriitis. Sometimes the musculature is involved in the sense of a polymyositis and the skin in the sense of a dermatomyositis. There are changes in the heart valves (endocarditis of Libman-Sacks), in the kidneys, in the spleen, and in the liver, the thymus, and other organs. Seldom is the full picture of the illness observed with simultaneous attack on all the indicated organs. Usually, and, above all, in the initial stage, only two or three organ manifestations are recognizable.

It is often difficult for the doctor to assign the symptoms to the attack of a single disease. The results of immunobiological investigation, however, allow one to hope that, even here, one can come to a uniform interpretation of the occurrences of the illness, which last but not least, will also benefit the therapeutic line of attack.

The disease strikes chiefly women in the younger and middle-aged groups. The course is chronically progressive. The duration of the disease may amount to, at the most, 8 to 10 years. The cause of death is not seldom a kidney failure. Spontaneous remissions are described, but, in general, they are rare. For the diagnosis, besides the clinical symptomatology, the histological tissue examination, as well as the determination of antibody factors in the serum of the patient, as well as also the positive L. E. cell phenomenon, are decisively important.

As so often in medicine, therapy tests are undertaken in etiologically unknown and pathogenically obscure diseases, which often show a surprising positive effect, but which also on the other hand permit conclusions on the occurrence of the disease and again spur on the exact and experimental investigations.

The case described in the following shows the course of the illness of a systemic Lupus erythematosus, in which, after negative results with the methods of treatment customarily used up to now, first a combined therapy of corticosteroids with a cytostat (Endoxan) brought a decisive turn in the course of the disease and a hardly expected result. The period of observation of this case extended over ten months, with initially 3 months of stationary treatment and, thereafter, 7 months of ambulatory treatment.

Similar good results were recorded by Seah, Wong, Chew, and Jayaratnam, as well as by Hill and Scott.

Description of the Case

The patient was a 27-year-old female with a chronically progressive course of a systemic Lupus erythematosus with predominant appearances of a polyarthritis, a scleroderma, and a Raynaud syndrome. She took sick in 1963, three months after a delivery, first of all with blood supply disturbances in the fingers, subsequently, joint involvement. According to the first diagnosis: initial stage of polyarthritis. Treatment with corticosteroids and other 'rheumatism treatments.' Only passing improvement. 1966 treatment in a clinic, in which, besides a Raynaud syndrome and a polyarthritis, also a beginning scleroderma was ascertained.

AST at 2400 I. E. strongly raised, L. E. Cell test, Waller-Rose test, and Latex test at that time negative. Treatment with penicillin and corticosteroids. Hardly any improvement. Increase of joint complaints. End of 1966, stationary treatment in a 'rheumatism clinic': corticosteroids, resochin, penicillin. For the first time, anti-nuclear factors detected in the serum.

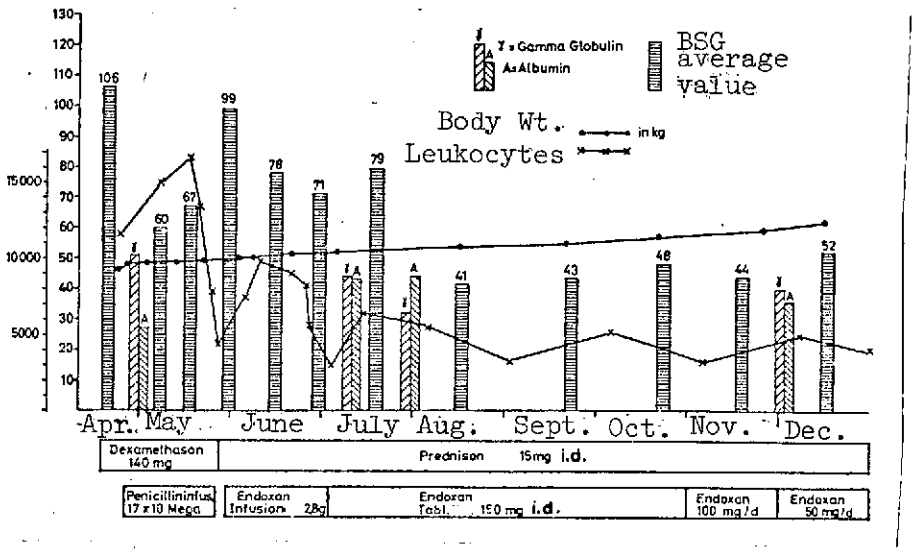
Further deterioration of condition during confinement. January 1967, therapy trial with sex hormones (Primolut). End of

1967, renewed stationary treatment in the 'rheumatism clinic.' Therapy trial with azathioprine (Imuran). Slight improvement. After release, the patient took sick in November 1967 with shingles. Imuran therapy discontinued because of that. Antibiotic and B_{12} therapy as well as corticosteroids. Increasing deterioration of condition. Loss of weight. Increasing stiffening of the hands. Constantly bedridden and needing care. Treatment attempts through homeopathy and through an unreliable 'radiation institute' in a foreign country. From April 16, 1968, stationary treatment in our hospital. The condition on admission amounted to full-time care. Strongly reduced nourishment and strength condition. Almost complete stiffening of the large and small joints, especially also the jaw joint. Tongue dry and chapped, partly coated, whitish. Features expressionless. Body weight 45.2 kg. Lungs and heart physically o. B. RR 140/80 mm Hg. Liver and spleen not demonstrably enlarged. Collapsed abdominal wall. Livid skin colors on the hands and feet. Trophic disturbances at the tops of the fingers. Hand muscle atrophy and indurations of the palmar aponeuroses on both sides. Temperature between 38° and 39°.

Leukocytosis in the early days between 11,600 and 16,600. Slight anemia. Urine: E+, sediment, o. B. BSG 140/145 mm n. W., AST 400 I. E. Latex-RF ϕ, Latex-CRP: +, L. E. Cell determination positive. Electrophoresis: Albumin 27.5, alpha-1-Globulin 1.5, alpha-2-Globulin 8.0, beta 11, gamma 57 rel. %.

We treated first with penicillin infusions, butazolidine, and dexamethasone (see the chart). In spite of the 17-day treatment, there was no objective or subjective improvement, disregarding a temporary reversal of the blood depression. We decided then on a combined corticosteroid-Endoxan treatment (see the chart). After that, a surprising improvement of the general state of health, normalization of the temperature, reversal of

the joint stiffening, increase of appetite and weight to 47.8 kg, improvement of the blood count, normalization of the leukocyte number, and considerable improvement of the electrophoresis, all took place.



The patient could again leave the bed, could again get dressed and undressed without outside help, and generally could get along with a cane. /367

Analyses at discharge: BSG: 84/116 mm n. W., AST 200 I. E., Latex-RF: ϕ, Latex-CRP: +, Leukocytes: 5200, Electrophoresis: Albumin 43.0, alpha-1-Globulin 2.0, alpha-2-Globulin 6.0, beta 5.0, gamma 44.0 rel. % (see also the chart).

On June 20, 1968, discharge from the hospital. Further treatment with Endoxan and prednisone under continuous ambulatory controls of the blood condition, the BGS, and the rheumatism factors, as well as the anti-streptolysin titer. Gradual reduction of the corticosteroid and Endoxan dosage. The patient felt comparatively good at the time, except for occasional joint

complaints. She looked after her household by herself. The menstruation which had been suspended for a year appeared again regularly. The body weight since release from the hospital climbed from 47.8 to 62.5 kg. No sign of Cushing's syndrome.

At the last control examination two weeks ago, a slight increase of the blood depression and an increase of the AST were observed. Whether this is the first sign of a deterioration or of a residue of the illness cannot yet be determined at this time. At the moment, the inclination towards leukopenia forbids an increase of the Endoxan dosage.

Summary

We report on an unusual treatment result of a systemic Lupus erythematosus with surprisingly good improvement of the course of the disease which was chronically progressive by itself, in an observation period of ten months, with a combined corticosteroid-Endoxan therapy, after which continuing attempts at treatment with corticosteroids alone or in combination with other medications used in rheumatic illnesses, and also the so-called 'immunosuppressive' substance azathioprine (Imuran) had no significant therapeutic effect.

At the present status of investigation in the field of autoimmune illnesses, of which the primary are para-rheumatic illnesses such as systemic Lupus erythematosus, it seems that an attempted treatment with the applied cytostatic therapy in combination with corticosteroids, for lack of better possibilities of treatment, is vindicated.

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